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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/564,647	07/19/2006	Philip David Monk	102789-1P US	1467
44992 7590 03/31/2009 ASTRAZENECA R&D BOSTON 35 GATEHOUSE DRIVE WALTHAM, MA 02451-1215				
EXAMINER				
SKELDING, ZACHARY S				
ART UNIT		PAPER NUMBER		
1644				
MAIL DATE		DELIVERY MODE		
03/31/2009		PAPER		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

10/564,647

**Applicant(s)**

MONK ET AL.

**Examiner**

ZACHARY SKELDING

**Art Unit**

1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 22 June 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1, 3-34, 41-58 and 61 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1, 3-34, 41-58 and 61 are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S5108)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

### **DETAILED ACTION**

1. Applicant's amendment filed June 22, 2007 is acknowledged.

Claims 2, 35-40, 59, 60 and 62-91 have been canceled.

Claims 1, 3, 9 and 14 have been amended.

Claims 1, 3-34, 41-58 and 61 are pending.

### ***Election/Restrictions***

2. Restriction is required under 35 U.S.C. 121 and 372.
3. This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1, 3 and 4-21, drawn to an isolated specific binding member for human IL-13 comprising an antibody antigen-binding site which is composed of a human antibody VH domain and a human antibody VL domain...

Group II, claim(s) 22, drawn to an isolated antibody VH domain of a specific binding member according to claim 1.

Group III, claim(s) 23, drawn to an isolated antibody VL domain of a specific binding member according to claim 1.

Group IV, claim(s) 26 and 27, drawn to isolated nucleic acid comprising a nucleotide sequence encoding a specific binding member or antibody Vh or Vl domain of a specific binding member according to claim 1, and host cells containing said nucleic acid.

Group V, claim(s) 28-30, drawn to methods of producing a specific binding member or antibody Vh or Vl domain.

Group VI, claim(s) 31-34, 41 and 49-55, drawn to a method for producing an antibody comprising providing, by way of addition, deletion, substitution or insertion of one or more amino acids in the amino acid sequence of a parent VH domain comprising HCDR 1, HCDR2 and HCDR3, wherein the parent VH domain HCDR1, HCDR2 and HCDR3 are the BAK278D6 set of HCDR's, defined wherein the HCDR1 has the amino acid sequence of SEQ ID NO: 1, the HCDR2 has the amino acid sequence of SEQ ID NO: 2, the HCDR3 has the amino acid sequence of SEQ ID NO: 3, or the BAK502G9 set of HCDR's, defined

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wherein the HCDR1 has the amino acid sequence of SEQ ID NO: 7, the HCDR2 has the amino acid sequence of SEQ ID NO: 8, the HCDR3 has the amino acid sequence of SEQ ID NO: 9, a VH domain which is an amino acid sequence variant of the parent VH domain, and optionally combining the VH domain thus provided with one or more VL domains to provide one or more VH/VL combinations; and testing said VH domain which is an amino acid sequence variant of the parent VH domain or the VH/VL combination or combinations to identify an antibody antigen binding domain specific for human IL-13.

Group VII, claim(s) 42-48, drawn to a method for producing a specific binding member that binds human IL-13, which method comprises: providing starting nucleic acid encoding a VH domain or a starting repertoire of nucleic acids each encoding a VH domain, wherein the VH domain or VH domains either comprise a HCDR1, HCDR2 and/or HCDR3 to be replaced or lack a HCDR1, HCDR2 and/or HCDR3 encoding region; combining said starting nucleic acid or starting repertoire with donor nucleic acid or donor nucleic acids encoding or produced by mutation of the amino acid sequence of the HCDR1 (SEQ ID NO: 1) or HCDR1 (SEQ ID NO: 7), HCDR2 (SEQ ID NO: 2) or HCDR2 (SEQ ID NO: 8) and/or HCDR3 (SEQ ID NO: 3) or HCDR3 (SEQ ID NO: 9) such that said donor nucleic acid is or donor nucleic acids are inserted into the CDR1, CDR2 and/or CDR3 region in the starting nucleic acid or starting repertoire, so as to provide a product repertoire of nucleic acids encoding VH domains; expressing the nucleic acids of said product repertoire to produce product VH domains; optionally combining said product VH domains with one or more VL domains; selecting a specific binding member specific for human IL-13, which specific binding member comprises a product VH domain and optionally a VL domain; and recovering said specific binding member or nucleic acid encoding it.

Group VIII, claim(s) 56-58, drawn to a method comprising binding a specific binding member that binds IL-13 according to claim 1 to human IL-13 or a fragment of human IL-13.

Group IX, claim 61, drawn to a method of treatment of a disease or disorder selected from the group consisting of asthma, atopic dermatitis, allergic rhinitis, fibrosis and Hodgkin's lymphoma, the method comprising administering a specific binding member according to claim 1 to a patient with the disease or disorder or at risk of developing the disease or disorder.

4. Claims 24 and 25 link(s) inventions I-III. The restriction requirement between the linked inventions is **subject to** the nonallowance of the linking claim(s), claim 24 and 25. Upon the indication of allowability of the linking claim(s), the restriction requirement as to the linked inventions **shall** be withdrawn and any claim(s) depending from or otherwise requiring all the limitations of the allowable linking claim(s) will be rejoined and fully examined for patentability in accordance with 37 CFR 1.104 **Claims that require all the limitations of an allowable linking claim** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final

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rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

Applicant(s) are advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, the allowable linking claim, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

5. The inventions listed as Groups I-IX do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: the inventions encompassed by the linking claims 24 and 25 and the claims of Groups I-III are not regarded as being of similar nature because these alternatives do not share a common structure. See MPEP § 1815.

In particular, it is accepted in the art that Vh and Vl containing specific binding members generated from, e.g., human or mouse Vh and Vl germline sequences and V(D)J recombination, generally require all of the heavy and light chain CDRs in the context of framework sequences which maintain their required conformation to bind antigen, proper association of heavy and light chain variable regions being required to form a functional antigen binding site (See Janeway et al., Immunobiology, 5<sup>th</sup> Ed., Garland Science, pp. 94-105 (2001)).

However, it is known in the art that isolated Vh domains can be prepared, for example in camels, which bind to antigen. However these isolated Vh antibodies have structural features that distinguish them from Vh and Vl containing specific binding members generated from, e.g., human or mouse Vh and Vl germline sequences and V(D)J recombination (see, e.g., Holt et al., Trends Biotechnol. 2003 Nov;21(11):484-90, in particular page 485, left column, 2<sup>nd</sup> paragraph).

Moreover, there is a lack of expectation in the art that these various alternatives will behave in the same way in the context of the claimed invention. For example, isolated Vh domains that bind to human IL-13 (or isolated Vl domains for that matter) are expected to have substantially shortened serum half-lives and further are expected to be successfully produced at high levels in microbial cells in contrast to specific binding members comprising Vh and Vl domains (see Holt, in particular, page 488, left column, 2<sup>nd</sup> paragraph to page 489).

6. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

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species of specific binding members for human IL-13 comprising particular Vh/Vl domains and/or particular HCCDR and LCCDR sequences, see, e.g., claims 1, 3, 13 and 14.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. For example, applicant may elect the species of specific binding member for human IL-13 "comprising the BAK502G9 Vh domain (SEQ ID NO: 15)", or "comprising the antibody of claim 1 with a substitution of Q at position 31 in HCDRI".

***The reply must also identify the claims readable on the elected species, including any claims subsequently added.*** For example, if applicant elects the species of specific binding member for human IL-13 "comprising the BAK502G9 Vh domain (SEQ ID NO: 15)" and this species corresponds some particular antibody identified in claim 3, applicant must indicate that claim 3 reads on the elected species if it is to be considered for examination.

An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

7. The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply

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where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

8. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).
9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ZACHARY SKELDING whose telephone number is (571)272-9033. The examiner can normally be reached on Monday - Friday 8:00 a.m. - 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Zachary Skelding/  
Examiner, Art Unit 1644  
March 28, 2009